56. (New) ~~A composition~~, comprising the neurotrophic variant of SEQ ID NO:34 according to Claim 51 and a physiologically acceptable carrier.

A3 cont'd

57. (New) The composition of Claim 56, further comprising a mammalian neurotrophic factor.

Subt B9

58. ~~(New) The composition of Claim 57, wherein said~~ neurotrophic factor is CNTF ~~or LIF~~.

REMARKS

Claims 1-24, 40 and 41 have been cancelled without prejudice. Claims 25, 26 and 29 have been amended and new Claims 42-58 have been added. Claims 25-39 and 42-58 are pending.

Claims 25 and 26 have been amended to more clearly define the claimed subject matter, and Claim 29 has been amended to correct an informality.

Support for the amino acid sequences recited in new Claim 42 is found throughout the specification, for example, at page 24, line 18 *et seq.*, and page 41, Table 1.

Support for new Claims 51-58 is found throughout the specification, for example, at page 21, line 16 *et seq.*, page 23, lines 4-17, and page 41, Table 1.

Further support for new Claim 53 is found at page 8, lines 19-20.

Further support for new Claim 54 is found at page 19, lines 15-19, and page 31, line 10 *et seq.*

Further support for new Claim 55 is found at page 23, lines 5-11.

New Claims 42-58 are drawn to the Group III invention, as defined in the Restriction Requirement.

The amended claims and new claims are supported by the application as originally filed. Therefore, this Amendment adds no new matter.

Reply to Restriction Requirement

Responsive to the Restriction Requirement dated September 4, 2002, the claims of Group III (Claims 25-39 in part), defined by the Examiner as being drawn to "peptides and peptide compositions," are elected for prosecution with traverse. Responsive to the further Restriction Requirement to elect a single peptide embodiment and a single mammalian neurotrophic factor, Applicants elect SEQ ID NO:12 as the peptide and CNTF as the mammalian neurotrophic factor.

Applicants reserve the right to file a continuing application or take such other appropriate action as deemed necessary to protect the non-elected inventions. Applicants do not hereby abandon or waive any rights in the non-elected inventions.

Reasons for Traverse and Proposed Modification of the Restriction Requirement

The Examiner restricted the claimed invention into the following for groups:

I. Claims 1-18 drawn to a method providing trophic support for neurons;

II. Claims 19-24 drawn to a method for stimulating the secretion of interleukin-6 in a mammal;

III. Claims 25-39 drawn to peptides and peptide compositions; and

IV. Claims 40 and 41 drawn to a method of providing trophic support for glial cells in a mammal.

The Examiners attention is drawn to Claims 30-33, 37 and 38 which are included in Group III. These claims are drawn to fusion proteins and compositions comprising the fusion proteins. The Examiner is requested to confirm that Claims 30-33, 37 and 38 are included in Group III.

In addition to election of one of Groups I-IV for examination on the merits, the Examiner further restricted the claims to single molecular embodiments selected from the following groups:

a single peptide embodiment selected from A) TS, B) C44 (SEQ ID NO:12), and TR1 (SEQ ID NO:32); and

a mammalian neurotrophic factor selected from A) CNTF and B) LIF.

It is noted that the groups of molecular embodiments listed in the Restriction Requirement do not include all proteins, peptides and variants that are disclosed or claimed. For example, Claim 25 as originally filed is drawn to a neurotrophic peptide comprising the amino acid sequence of peptide C14 (SEQ ID NO:14) or a neurotrophic variant thereof.

The further restriction to single molecular embodiments appears to have been issued because the identified proteins, peptides and variants are patentably distinct, and in the Examiner's opinion, "searching all of the molecules in a single patent application would provide an undue search burden on the examiner and the USPTO's resources because the indicated searches are not co-extensive." (Restriction Requirement at page 4, lines 9-11.)

Relationships Among Disclosed Neurotrophic Amino Acid Sequences

The application discloses the amino acid sequences of several peptides derived from and variants of *T. cruzi* trans-sialidase (TS) that have neurotrophic or IL-6 secretion inducing activity. The disclosed amino acid sequences can be divided into groups that share common biological activity (neurotrophic or IL-6 secretion inducing activity) and a common "core sequence." In particular, the application discloses the amino acid sequences of two clones of TS: SEQ ID NO: 2 and SEQ ID NO:34. The application also discloses amino acid sequences of neurotrophic peptides and neurotrophic variants, and the amino acid sequences of IL-6 secretion inducing peptides and IL-6 secretion inducing variants, that are encompassed by SEQ ID NO:2 or SEQ ID NO:34.

For example, the application discloses that neurotrophic peptides C14 (SEQ ID NO:14), CFN1 (SEQ ID NO:13) and C44 (SEQ ID NO:12) are derived from TS encoded by clone 7F (SEQ ID NO:34). (Specification at page 41, lines 12-14.) In fact, SEQ ID NO:14 is amino acid residues 379-394 of SEQ ID NO:34, and thus, is encompassed by SEQ ID NO:34 and by neurotrophic variants of SEQ ID NO:34 that comprise amino acid residues 379-394, such as TS-F (amino acids 33-666 of SEQ ID NO:34) and TS-F-47 (amino acids 79-666 of SEQ ID NO:34).

(Specification at page 19, lines 18-19, and page 8, lines 19-20, respectively.) SEQ ID NO:14 is also encompassed by peptide CFN1 (SEQ ID NO:13) and a variant of SEQ ID NO:14 containing a single inserted amino acid is encompassed by peptide C44 (SEQ ID NO:12).

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R Q R L P K R M G G S Y R C                    SEQ ID NO:14
R Q R L P K R M G G S Y R C VNASTAH             SEQ ID NO:13

                  R Q R L P - K R M G G S Y R C          SEQ ID NO:14
QPLRRQRVVVVPLSPRLVLLAFC R Q R L P L K R M G G S Y R C VNASTAN    SEQ ID NO:12
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A similar situation exists for neurotrophic peptides C19Y21 (SEQ ID NO:15) and CYN2 (SEQ ID NO:16), and neurotrophic variants TS-F (amino acids 33-666 of SEQ ID NO:2) and TS-CC-47 (amino acids 79-478 of SEQ ID NO:2) which are derived from TS encoded by clone 19Y (SEQ ID NO:2).

Proposed Modification or Rejoinder

Applicants propose that the disclosed embodiments of the invention of Group III could be further restricted by requiring an election of a patentably distinct species to which the claims would be restricted if a generic claim is not found to be allowable. Alternatively, if under current PTO practice the Examiner prefers to view the disclosed embodiments of the invention of Group III as separate inventions, the full scope of any generic claim that reads on the elected single molecular embodiment and links two or more such embodiments should be examined. If such a linking claim is found to be allowable, claims drawn to single molecular embodiments that are linked by that linking claim should be rejoined.

1. Modification to Reflect Genus/Species Relationship

Claims 25 and 34 as filed are generic. If Group III is viewed as genus/species, Applicants would be required to elect a species selected from A) neurotrophic peptide or variant and compositions comprising same, or B) IL-6 secretion inducing peptide or variant and compositions comprising same.

If A) is elected, Applicants would make a further election of a single disclosed neurotrophic species, to which the claims would be restricted if no generic claim is found to be allowable, selected from:

SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, amino acids 33-666 of SEQ ID NO:34, and amino acids 79-666 of SEQ ID NO:34.

If B) is elected, Applicants would make a further election of a single disclosed IL-6 secretion inducing species, to which the claims would be restricted if no generic claim is found to be allowable, selected from:

SEQ ID NO: 32, SEQ ID NO:26, SEQ ID NO: 27, SEQ ID NO:28, SEQ ID NO:29 and amino acids 667-1162 of SEQ ID NO:34.

B. Rejoinder

Alternatively, if the Examiner maintains that the disclosed embodiments of Group III are separate inventions and should be further restricted to single molecular embodiments, Applicants propose that the single molecular embodiment to be examined be selected from the disclosed neurotrophic embodiments and the disclosed IL-6 secretion inducing embodiments:

neurotrophic embodiments: SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14, amino acids 33-666 of SEQ ID NO:34, amino acids 79-666 of SEQ ID NO:34; and

IL-6 secretion inducing embodiments: SEQ ID NO: 32, SEQ ID NO:26, SEQ ID NO: 27, SEQ ID NO:28, SEQ ID NO:29 and amino acids 667-1162 of SEQ ID NO:34.

It is pointed out that original Claim 25 and new Claim 51 are generic claims that link inventions consisting of individual neurotrophic molecular embodiments, and original Claim 34 is a generic claim that links inventions consisting of individual IL-6 secretion inducing molecular embodiments. (See, MPEP § 809.03 at 800-52 (8th ed., Aug., 2001)). When a linking claim is present, the Manual of Patent Examining Procedure instructs that:

> The linking claim must be examined with the invention elected, and should any linking claim be allowed, the restriction requirement must be withdrawn. Any claim(s) directed to the nonelected invention(s), previously withdrawn from
>
> consideration, which depends from or includes all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability.

MPEP § 809 at 800-48 (8th ed., Aug., 2001).

Therefore, in accordance with the policy outlined in the MPEP, a linking claim that reads on the elected invention should be examined, and if found to be allowable, claims drawn to individual molecular embodiments that are linked by the examined linking claim should be rejoined.

It is also pointed out that none of the single molecular embodiments defined in the Restriction Requirement, or even a collection of all of those embodiments, encompass the full scope of Applicants' invention as claimed in original Claim 25 or original Claim 34. Thus, examination of a linking claim will ensure that Applicants' invention is examined on the merits, and comports with the holding of the Court of Customs and Patent Appeals in Weber:

> [A]n applicant has a right to have *each* claim examined on the merits. If an application submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications .... If, however, a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits. The totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim. Further, since the subgenera would be defined by the examiner rather than by the applicant, it is not inconceivable that a number of the fragments would not be described in the specification.

In re Weber, Soder and Boksay, 198 USPQ 328, 331 (CCPA 1978).

Therefore, in accordance with MPEP § 809 and Weber, any linking claims that read on the elected single molecular embodiment should be examined, and if found to be allowable, claims drawn to additional molecular embodiments linked by such linking claims should be rejoined.

Reasons that Applicants' Suggested Modification or Rejoinder Should be Adopted

The proposed modification or rejoinder should be adopted because it comports with the PTO's goals of providing compact and efficient examination. Further, in view of the relationship of the amino acid sequences of the disclosed embodiments discussed above, examination of generic Claims 25 and 51, or generic Claim 34, under genus/species procedures or under linking claim procedures will not produce an undue burden on PTO resources or the Examiner.

For example, if SEQ ID NO:14 is elected as the species or as the single molecular embodiment, Claims 25 and 51 should be examined to the extent they read on SEQ ID NO:14. If found to be allowable to that extent, the full scope of the claims could be examined without undue burden. Expanding examination would not be unduly burdensome because an initial search designed to identify prior art relevant to amino acid sequences that comprise the "core sequence" of SEQ ID NO:14 will identify prior art that is relevant to the examination of additional embodiments which comprise that "core sequence." Thus, such a search would be sufficient for examination of Claims 25 and 51 to the extent they read on embodiments that comprise SEQ ID NO:14, and any further search that the Examiner considers necessary to examine the full scope of Claims 25 and 51 could easily be conducted.

Thus, the proposed modification/rejoinder comports with United States Patent Office Procedure as stated in the Manual of Patent Examining Procedure:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

(MPEP § 803 at 800-3 (8th ed., Aug. 2001)).

In addition, the proposed modification or rejoinder should be adopted because doing so will relieve Applicants of the oppressive burden of filing multiple applications, each containing claims drawn only to a single molecular embodiment, that is imposed by the current Restriction Requirement, without imposing a serious burden on the Examiner. Again, it is noted that the Weber court appreciated that Applicants for patents may not be able to obtain adequate protection for their inventions if they are required to file multiple applications that only contain claims drawn to single embodiments.

Summay and Elections

As stated above, the claims of Group III (Claims 25-39), are elected for prosecution with traverse. Responsive to the further Restriction Requirement to elect a single peptide embodiment and a single mammalian neurotrophic factor, Applicants elect SEQ ID NO:12 as the peptide and CNTF as the mammalian neurotrophic factor.

1. If the Examiner adopts the proposed genus/species classification, Applicants elect the

Claims of Group III and further elect claims drawn to a neurotrophic peptide or variant and compositions comprising same, and SEQ ID NO:14 as the species of neurotrophic peptide or variant, and CNTF as the mammalian neurotrophic factor.

Claims 25-33 and 42-58 read on the elected species.

2. If the Restriction Requirement is maintained in its current form, Applicants respectfully

request that the list of single peptide embodiments presented in the Restriction Requirement be expanded to include all disclosed embodiments.

If this request is granted, Applicants elect the claims of Group III, and further elect SEQ ID NO:14 as the peptide embodiment, and CNTF as the mammalian neurotrophic factor.

Claims 25 and 51 are generic linking claims that link the elected invention (SEQ ID NO:14) and the inventions of Claims 26-33 and 42-50, and 52-58, respectively. Examination of Claims 25 and 51 is requested for the reasons discussed above.

Information Disclosure Statement

An Information Disclosure Statement (IDS) is being filed concurrently herewith. Entry of the IDS is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

Claims 1-24, 40 and 41 have been canceled, and new Claims 42-58 have been added to the application.

25. (Amended) A neurotrophic peptide, comprising the amino acid sequence of peptide C14 (SEQ ID NO:14) or a neurotrophic variant [thereof] of SEQ ID NO:14, wherein said neurotrophic variant has at least 90% amino acid sequence identity to SEQ ID NO:14.

26. (Amended) The peptide of Claim 25, further comprising an amino-terminal protecting group, a carboxyl-terminal protecting group, or [a combination thereof] an amino-terminal protecting group and a carboxyl-terminal protecting group.

29. (Amended) The composition of Claim 28, wherein said neurotrophic factor is CNTF [of] or LIF.